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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,296	06/28/2004	Yuji Yamazaki	081356-0218	7715

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EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
07/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,296	YAMAZAKI ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2008 and 12 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *1,2,4 and 6* is/are withdrawn from consideration.

5)☒ Claim(s) *20-22* is/are allowed.

6)☒ Claim(s) *23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 19, 2008 has been entered.

2. Applicant's amendment and remarks filed March 19, 2008 are acknowledged.

   Claims 22 and 23 have been amended.

   Claims 3, 5 and 7-19 have been canceled.

   Claims 1, 2, 4 and 6 have been withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being directed to a non-elected Species.

   Claims 1, 2, 4, 6 and 20-25 are pending.

   Claims 20-25 are under examination as they read on "anti-FGF-23 antibodies that bind amino acid 25-179 of SEQ ID NO:1".

3. This Office Action is in response to applicant's amendment and remarks filed July 30, 2007.

   The prior rejections of record can be found in the Office Action mailed October 19, 2007.

   The prior rejection under 35 U.S.C. § 112, 1st paragraph put forth in the Office Action mailed October 19, 2007 is withdrawn in view of applicant's amendment to the claims.

   The prior obviousness-type double patenting rejection has been withdrawn in view of changes to the claims of the reference application.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

   > A person shall be entitled to a patent unless –
   >
   > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 23-25 stand rejected under 35 U.S.C. § 102(b) as anticipated by Itoh et al. (WO 01/66596, cited on applicant's IDS of June 28, 2004), as evidenced by Yu et al. (Endocrinology. 2005 Nov;146(11):4647-56) and Mohammadi et al. (Cytokine Growth

Factor Rev. 2005 Apr;16(2):107-37), essentially for the reasons of record as put forth in the Office Action mailed October 19, 2007.

Applicant has submitted experimental evidence showing that the 2C3B antibody, which binds an epitope localized within amino acids 25-179 of SEQ ID NO: 1, inhibits FGF-23 induced signaling while the 2A2B antibody, which binds amino acids 148-163 of SEQ ID NO: 1, does not inhibit FGF-23 induced signaling. On this basis applicant argues "[t]hus, antibodies binding to the sequence of amino acid residues 1-179 of FGF-23 do not "inherently" possess the property of neutralizing FGF-23 activity. Because the Examiner's rejection is based on a faulty rationale, withdrawal of the anticipation rejection is warranted."

Applicant's argument has been considered, but has not been found convincing, essentially for the reasons of record as put forth in the Office Action mailed October 19, 2007.

The prior art does not only teach "antibodies binding to the sequence of amino acid residues 1-179 of FGF-23."

Rather, the prior art (Itoh) teaches that FGF-23 is proteolytically cleaved into two fragments, one of which comprises from amino acid 1 to around 179, that polyclonal or monoclonal antibodies can be generated against this fragment via "any suitable method known in the art…[f]or example, murine or human monoclonal antibodies can be produced by hybridoma technology…," and that said antibodies can be used for "preventing or treating diseases involving overexpression of the FGF-23 protein," such as "X-linked Hypophosphatemic rickets" (see Itoh page 18, 3rd to 4th paragraphs, page 30, 4th to 5th paragraphs and page 31, 3rd paragraph).

Thus, the prior art teaches antibodies that bind amino acids 1 to around 179 of SEQ ID NO: 1 and that block FGF-23 activity, for example in a bioassay (see Itoh, in particular page 30, 4th to 5th paragraphs and page 31, 1st-3rd paragraphs). The fact that a particular antibody which binds amino acid residues 148-163 of SEQ ID NO: 1 does not antagonize FGF-23 induced signaling does not negate the logic of the prima facie case of anticipation put forth in the previous Office Action mailed October 19, 2007 because the prima facie case of anticipation is based on the prior art antibodies both binding to amino acid residues 1-179 of FGF-23 AND antagonizing FGF-23 activity.

More particularly, given that the antibodies of Itoh bind amino acids 1 to around 179 of FGF-23, and given that the antibodies of Itoh, like the instantly claimed antibodies, can be used to treat hypophosphatemic diseases involving overexpression of FGF-23, such as X-linked Hypophosphatemic rickets, and further given the highly conserved receptor binding surface of the FGF molecules, including FGF-23, as evidenced by Wu and Mohammadi (described in greater detail in the Office Action of January 30, 2007), the antibodies of Itoh would inherently compete with the instantly claimed antibodies.

Put another way, applicant still has not put forth a convincing argument that one of ordinary skill in the art, following the teachings of Itoh, would not make antibodies and pharmaceutical compositions as claimed.

Thus, the instant claims stand rejected as anticipated by Itoh as evidenced by Yu and Mohammadi.

Since the Office does not have a laboratory to test the reference antibodies and determine if they compete with the instantly claimed antibodies, it is applicant's burden to show that the reference antibodies are not competitive with the instantly claimed antibodies. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

Applicant is reminded that as stated in MPEP § 2112.01, "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)."

6. Claims 20-22 are allowable.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
July 21, 2008

/Michail A Belyavskyi/
Primary Examiner, Art Unit 1644